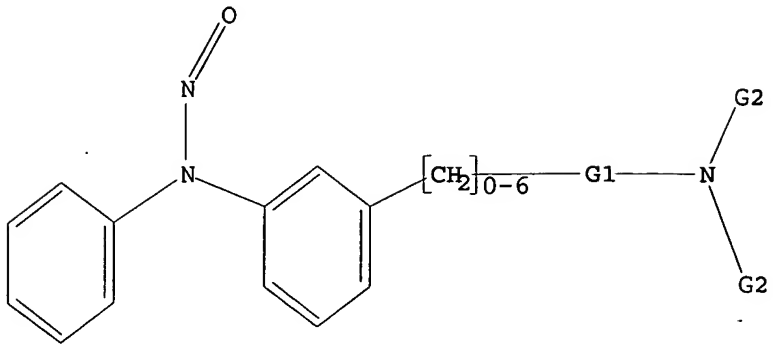
```
=> d his

     (FILE 'HOME' ENTERED AT 17:14:21 ON 03 OCT 2006)

     FILE 'REGISTRY' ENTERED AT 17:14:40 ON 03 OCT 2006
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           9 S L1 FULL

     FILE 'HCAPLUS, CHEMCATS' ENTERED AT 17:15:31 ON 03 OCT 2006
L4           4 S L3

     FILE 'HCAPLUS, HCAOLD, USPATFULL, EPFULL' ENTERED AT 17:18:02 ON 03 OCT
     2006
L5       40621 S ?DIPHENYLAMINE OR ?BIPHENYLAMINE
L6        2356 S L5 AND NITROSO
L7        1327 S L6 AND DERIVATIVE?
L8          37 S L7 AND (OXIDATIVE STRESS OR NITRIC OXIDE)
```

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 SO2,[@1]
G2 H,Cb,Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 17:15:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 34 TO ITERATE

100.0% PROCESSED 34 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 331 TO 1029
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

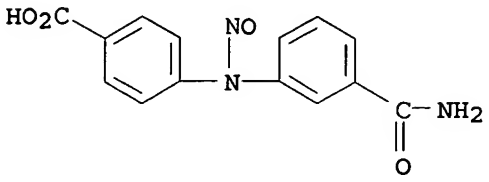
=> s l1 full
FULL SEARCH INITIATED 17:15:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 672 TO ITERATE

100.0% PROCESSED 672 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

L3 9 SEA SSS FUL L1

=> d scan

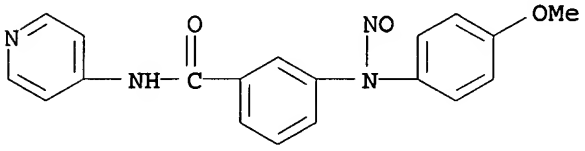
L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzoic acid, 4-[[3-(aminocarbonyl)phenyl]nitrosoamino]- (9CI)
MF C14 H11 N3 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

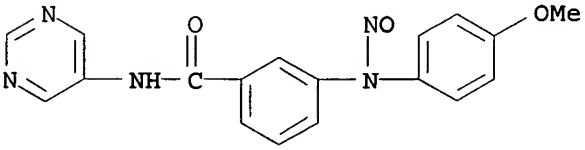
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):8

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-4-pyridinyl- (9CI)
MF C19 H16 N4 O3



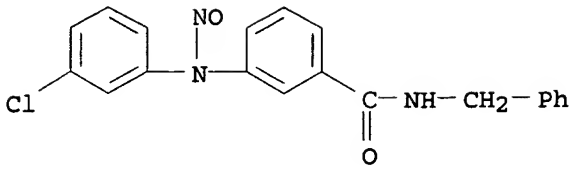
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-5-pyrimidinyl- (9CI)
MF C18 H15 N5 O3



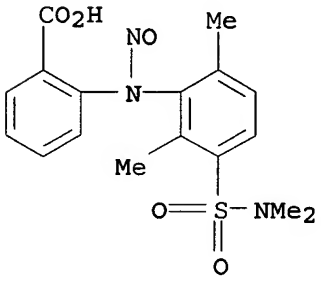
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(3-chlorophenyl)nitrosoamino]-N-(phenylmethyl)- (9CI)
MF C20 H16 Cl N3 O2



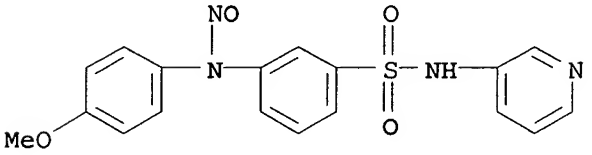
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Anthranilic acid, N-[3-(dimethylsulfamoyl)-2,6-xylyl]-N-nitroso- (8CI)
MF C17 H19 N3 O5 S



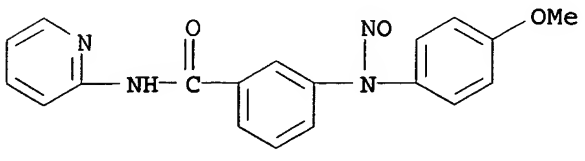
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzenesulfonamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-3-pyridinyl- (9CI)
MF C18 H16 N4 O4 S



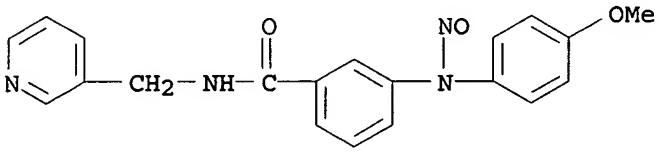
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-2-pyridinyl- (9CI)
MF C19 H16 N4 O3



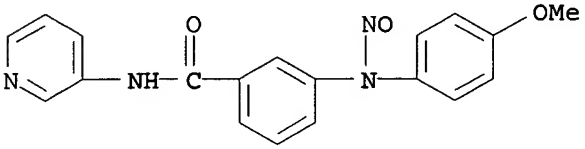
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-(3-pyridinylmethyl)- (9CI)
MF C20 H18 N4 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-3-pyridinyl- (9CI)
MF C19 H16 N4 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file hcaplus chemcat

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'HCAPLUS' ENTERED AT 17:15:31 ON 03 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'CHEMCATS' ENTERED AT 17:15:31 ON 03 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

=> s l3
L4 4 L3

=> d 1-4 ibib abs hitstr

L4 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:470967 HCAPLUS
DOCUMENT NUMBER: 143:26363

10/507,107

TITLE: Preparation of nitroso derivatives of diphenylamine as antioxidants and spontaneous nitric acid donors, pharmaceutical compositions containing them, and their use in the treatment of pathologies characterized by oxidative stress

INVENTOR(S): Lardy, Claude; Guedat, Philippe; Caputo, Lidia
PATENT ASSIGNEE(S): Merck Sante, Fr.

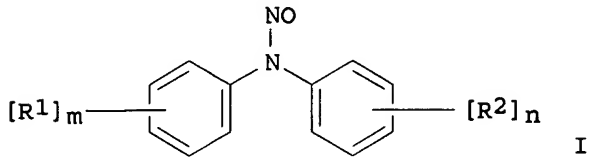
SOURCE: Fr. Demande, 63 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2862966	A1	20050603	FR 2003-13953	20031127
AU 2004293189	A1	20050609	AU 2004-293189	20041117
CA 2547282	AA	20050609	CA 2004-2547282	20041117
WO 2005051896	A1	20050609	WO 2004-EP14892	20041117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1687260	A1	20060809	EP 2004-804474	20041117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

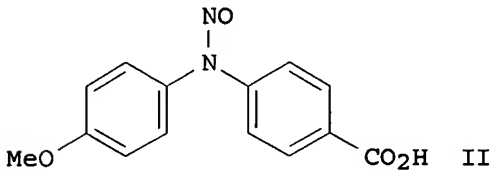
PRIORITY APPLN. INFO.: FR 2003-13953 A 20031127
WO 2004-EP14892 W 20041117

OTHER SOURCE(S): MARPAT 143:26363

GI



I



II

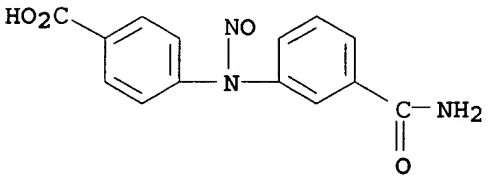
AB The invention relates to compds. I [wherein R1 = independently halo, CN, NH2, (un)substittued alkyl optionally interrupted by O or S, etc.; R2 = independently CN, OH, alkylcarbonyl, CO2H and derivs., etc.; n, m =

independently 1-5; with the exception of the compds. for which i = j = 1, R1 = CO2H, R2 = alkoxycarbonyl or R1 = CF3 and R2 = CO2H; and their derivs., salts, solvates, stereoisomers and pharmaceutically acceptable salts, including their mixts. in all proportions]. I are useful in the treatment of pathologies which are characterized by a condition of oxydative stress, and a deficit of the availability of endothelial nitric oxide (NO). I are generally prepared via the corresponding diphenylamines. Thus, reacting N-(4-methoxyphenyl)formamide with Et 4-fluorobenzoate, followed by saponification of the ester (no data), and nitrosation with NaNO2 in AcOH/H2O gave II (m.p. = 169-171°). At 150 μM in a test solution, compds. I spontaneously liberated NO, giving a colorimetric nitrate-nitrite level of 38-108 μM. In an in vitro test for antioxidant effect on the cupric ion-induced oxidation of human LDL in vitro, II had an IC50 of 17.0 μM. II reduced triglycerides by 58% in Zucker fatty rats after its administration for 8 days at 200 mg/kg/day/p.o.

IT 852931-28-3P, 4-[[3-(Aminocarbonyl)phenyl](nitroso)amino]benzoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-nitrosodiphenylamines and analogs as antioxidants for treatment of oxidative stress and related pathol.)

RN 852931-28-3 HCAPLUS

CN Benzoic acid, 4-[[3-(aminocarbonyl)phenyl]nitrosoamino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:719203 HCAPLUS

DOCUMENT NUMBER: 139:245765

TITLE: Nitroso derivatives of diphenylamine and pharmaceutical compositions containing them as drugs useful in the treatment of pathologies characterized by oxidative stress

INVENTOR(S): Lardy, Claude; Festal, Didier; Caputo, Lidia; Guerrier, Daniel

PATENT ASSIGNEE(S): Lipha, Fr.

SOURCE: Fr. Demande, 88 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2836917	A1	20030912	FR 2002-3025	20020311
FR 2836917	B1	20060224		
CA 2478652	AA	20030918	CA 2003-2478652	20030212
WO 2003076406	A1	20030918	WO 2003-EP1370	20030212

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003205756	A1	20030922	AU 2003-205756		20030212
EP 1483242	A1	20041208	EP 2003-702625		20030212
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BR 2003008338	A	20050201	BR 2003-8338		20030212
CN 1639126	A	20050713	CN 2003-805734		20030212
US 2005154232	A1	20050714	US 2003-507107		20030212
JP 2005533002	T2	20051104	JP 2003-574627		20030212
ZA 2004008109	A	20051020	ZA 2004-8109		20041007
PRIORITY APPLN. INFO.:			FR 2002-3025	A	20020311
			WO 2003-EP1370	W	20030212

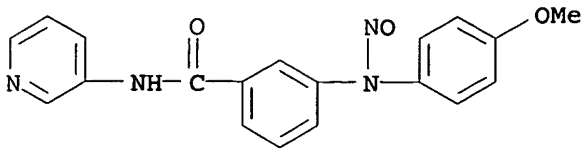
OTHER SOURCE(S): MARPAT 139:245765
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

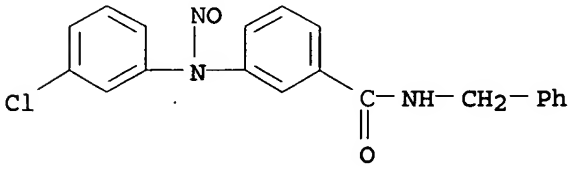
AB The invention relates to compds. I [wherein: each core Ph group is optionally substituted one or more times; n = 0, 1, 2, 3, 4, or 5; W = CO or SO2; Z = H, alkyl, aryl, or arylalkyl; R1 = any monovalent organic group; and pharmaceutically acceptable salts]. I are useful in the treatment of pathologies which are characterized by a condition of oxydative stress, and a deficit of the availability of endothelial nitric oxide (NO). I are generally prepared via the corresponding diphenylamines. Some of these diphenylamine precursors are also useful as medicinal antioxidants. Both I and the diphenylamines are useful for preparing medicaments for treating the metabolic syndrome of insulin resistance. For instance, Pd(0)-catalyzed coupling of 4-bromo-N-(pyridin-3-yl)benzamide with 4-methoxyaniline gave a diphenylamine derivative, 4-[(4-methoxyphenyl)amino]-N-(pyridin-3-yl)benzamide (II) in 55.9% yield. Nitrosation of II with aqueous NaNO2 in AcOH at room temperature gave 96.9% nitrosamine III. At 150 μM in a test solution, compds. I spontaneously liberated NO, giving a colorimetric nitrate-nitrite level of 46-108 μM. In a test for antioxidant effect on the cupric ion-induced oxidation of human LDL in vitro, III had an IC50 of 4.6 μM.

IT 600169-21-9P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(pyridin-3-yl)benzamide 600170-50-1P, 3-[1-(3-Chlorophenyl)-2-oxohydrazino]-N-(phenylmethyl)benzamide 600170-51-2P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(3-pyridylmethyl)benzamide 600170-52-3P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(5-pyrimidinyl)benzamide 600170-53-4P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(2-pyridyl)benzamide 600170-54-5P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(4-pyridyl)benzamide 600170-58-9P, 3-[1-(4-Methoxyphenyl)-2-oxohydrazino]-N-(3-pyridyl)benzenesulfonamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antioxidant and NO donor; preparation of N-nitrosodiphenylamines and analogs as antioxidants for treatment of oxidative stress and related pathol.)

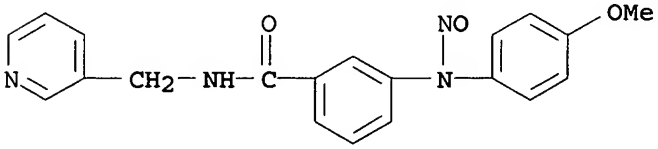
RN 600169-21-9 HCAPLUS
CN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 600170-50-1 HCAPLUS
CN Benzamide, 3-[(3-chlorophenyl)nitrosoamino]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 600170-51-2 HCAPLUS
CN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 600170-52-3 HCAPLUS
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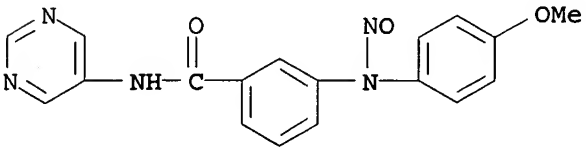
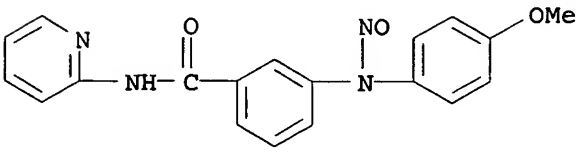
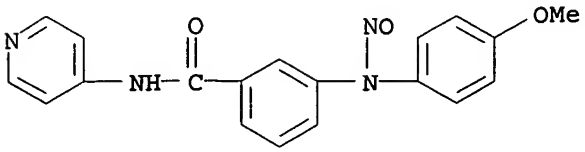


RN 600170-53-4 HCAPLUS
CN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-2-pyridinyl- (9CI) (CA INDEX NAME)

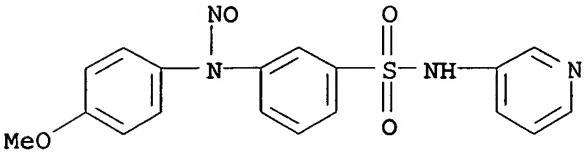


RN 600170-54-5 HCAPLUS

CN Benzamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 600170-58-9 HCAPLUS
CN Benzenesulfonamide, 3-[(4-methoxyphenyl)nitrosoamino]-N-3-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:100697 HCAPLUS
DOCUMENT NUMBER: 72:100697
TITLE: Antiinflammatory (1-substituted-3-indazolyloxy)acetic acids
INVENTOR(S): Palazzo, Giuseppe
PATENT ASSIGNEE(S): Aziende Chimiche Riunite Francesco Angelini
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3470194	A	19690930	US 1968-731723	19680524
IL 28032	A1	19710825	IL 1967-28032	19670523
GB 1152885	A	19690521	GB 1967-1152885	19670525
DK 115996	B	19691201	DK 1967-2769	19670526
ES 341123	A1	19680701	ES 1967-341123	19670529
BE 699226	A	19671103	BE 1967-699226	19670530
NL 6707510	A	19680301	NL 1967-7510	19670530
NO 118028	B	19691027	NO 1967-168378	19670530
SE 326451	B	19700727	SE 1967-7572	19670530
CH 504442	A	19710315	CH 1967-504442	19670530
FR 7174	M	19690811	FR 1967-7174	19670929
FR 2009259	A5	19700130	FR 1969-16894	19690523
DE 1926359	A	19700521	DE 1969-1926359	19690523
GB 1241637	A	19710804	GB 1969-1241637	19690523
US 27253	E	19711221	US 1970-10670	19700126
ES 544464	A3	19860116	ES 1985-544464	19850624

PRIORITY APPLN. INFO.:

IT 1966-21810	A	19660829
IT 1966-19723	A	19660829
IT 1967-15267	A	19670421
US 1968-731723	A	19680524

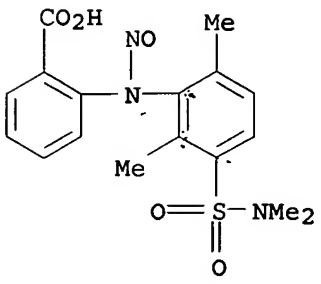
GI For diagram(s), see printed CA Issue.

AB By reacting certain metal salts of 3-hydroxyindazoles with halogenated aliphatic compds., antiinflammatory (3-indazolyloxy)alkanoic acids (I) and their salts were prepared An aqueous solution of the K salt of 1-(p-chlorobenzyl)-3-hydroxyindazole is prepared by dissolving 25.8 g of the indazole in 200 ml 14% KOH solution The aqueous solution is heated on a water-bath and 35 g monobromoacetic acid is added. Stirring and heating are continued until the pH of the solution is about 7 to give [1-(+-chlorobenzyl)-3-indazolyl]oxyacetic acid m. 117°. Prepared similarly were 1-(m-chlorobenzyl)-3-indazolyloxyacetic acid, m. 109° (which was prepared via the Et ester, b1.5 218°); (1-benzyl-3-indazolyloxy)acetic acid, m. 160°; (1-benzyl-3-indazolyl)oxyacetic acid, m. 160°; β-(1-benzyl-3-indazolyl)oxypropionic acid, m. 135°; (1-benzyl-5-nitro-3-indazolyl)oxyacetic acid, m. 155°; 5-amino-1-benzyl-3-indazolyl)oxyacetic acid, m. 217° (decomposition); (5-acetamido-1-benzyl-3-indazolyl)oxyacetic acid, m. 238°; [1-(2,6-dimethyl-3-dimethylsulfamoyl)phenyl-3-indazolyl]oxyacetic acid, m. 120-1°. Metallic salts of 1-benzyl-3-indazoleacetic acid prepared were (m.p. given): Zn, 110°; Pb, 170-73°; Al, 160°; Cd, 135-40°; Ca, 126-30°; Sn, 80-90°; Ag, 207°; Bi, 156°. Addition salts of (1-benzyl-3-indazoleacetic acid were prepared from NH4OH and from organic amines (m.p. given): NH4, 155°; N-hydroxymorpholine, 95-7°; piperazine, 175°; triethanolamine, 87-9°; ethylenediamine; morpholine, 137°; diethanolamine, 99°. [1-(m-Chlorobenzyl)-3-indazolyl]oxyacetic acid with diisopropylamine salt m. 109° and diethanolamine salt m. 106°. Also prepared were: [1-(2,6-dimethylphenyl)-3-indazolyl]oxyacetic acid, m. 130°; [1-(2,3-dimethylphenyl)-3-indazolyl]oxyacetic acid, m. 142°; (1-phenyl-3-indazolyl)oxyacetic acid, m. 164°; [1-(m-chlorophenyl)-3-indazolyl]oxyacetic acid, m. 148°; β-(1-phenyl-3-indazolyl)oxypropionic acid, m. 131°; β-(3-indazolyl)-oxypropionic acid, m. 179°; β-[1-(p-fluorophenyl)-3-indazolyl]-oxypropionic acid, m. 150-2°; [1-(o-chlorobenzyl)-3-indazolyloxyacetic acid, m. 156°; β-[1-(m-bromophenyl)-3-indazolyl]-oxypropionic acid, m. 89°; β-(5-methoxy-3-indazolyl)oxypropionic acid, m.p. 184; [1-(m-trifluoromethylphenyl)-3-indazolyl]-oxyacetic acid, m. 157°; (5-chloro-1-benzyl-3-indazolyl)oxyacetic acid, m. 158°; β-[1-(2,6-dimethyl)phenyl-3-indazolyl]-oxypropionic acid, m. 133°, (5-amino-1-benzyl-3-indazolyl)-oxyacetic acid-HCl, m. 230°; and 1-benzyl-6-chloro-3-indazolyloxyacetic acid, m. 157°. Formulations, including ointments and a lotion, are described.

IT 23864-74-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23864-74-6 HCAPLUS

CN Anthranilic acid, N-[3-(dimethylsulfamoyl)-2,6-xylyl]-N-nitroso- (8CI) (CA INDEX NAME)



L4 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:461380 HCAPLUS
DOCUMENT NUMBER: 71:61380
TITLE: (Indazol-3-yloxy)alkanoic acids
PATENT ASSIGNEE(S): Aziende Chimiche Riunite Francesco Angelini
SOURCE: Fr., 6 pp.
CODEN: FRXXAK
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LANGUAGE: French
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1530097		19680621	FR 1967-112773	19670630
DE 1645971			DE	
FR 7174			FR	
GB 1152885			GB	
PRIORITY APPLN. INFO.:			IT	19660829
			IT	19670421

OTHER SOURCE(S): MARPAT 71:61380
GI For diagram(s), see printed CA Issue.
AB Title compds. (I) where X = H, Cl, OMe, NO2, NH2, or NHCOMe, R = H, Ph (substituted, or not), or benzyl (substituted, or not), and n = 1 or 2, having interesting pharmacol. properties, are prepared Bromoacetic acid (35 g.) is added to a refluxing solution of 25.8 g. 1-(p-chloro)benzyl-3-hydroxyindazole in 200 cc. 14% KOH. The solution is heated at 100° with stirring until the pH is 7, cooled, filtered, and acidified to give α-[1-(p-chloro)benzyl-3-indazolyl]oxyacetic acid, m. 117°. A mixture of 246 g. Na salt of 1-benzyl-3-hydroxyindazole (II), 131 g. chloroacetamide, and 1 l. dioxane is refluxed for 2 hrs., and the solvent evaporated in vacuo to give α-(1-benzyl-3-indazolyl)oxyacetamide (III), m. 135-7°. A mixture of 155 g. III, 300 cc. dioxane, and 300 cc. concentrated HCl is refluxed for 2 hrs., cooled, and diluted with water to give α-(1-benzyl-3-indazolyl)oxyacetic acid (IV), m. 160°. A solution of 5.2 g. chloroacetonitrile in 5 cc. absolute EtOH is added with stirring to a refluxing solution of 11 g. II in 70 cc. anhydrous EtOH. The mixture is refluxed for 45 min., cooled, filtered, and the solution concentrated in vacuo to give α-(1-benzyl-3-indazolyl)oxyacetonitrile (V), m. 93°. A mixture of 1 g. V and 5 cc. concentrated HCl is heated at 100° for 2-3 min., cooled, and the precipitate worked up to give IV. A mixture of 28.1 g. Na salt of 1-(m-chloro)benzyl-3-hydroxyindazole, 16.7 g. ethyl bromoacetate, and 280 cc. 1,2-dimethoxyethane is heated at 100° with stirring for 3 hrs. to give a mixture of Et α-[1-(m-chloro)benzyl-3-indazolyl]oxyacetate, and Et α-[1-(m-chloro)benzyl-3-oxo-2-indazolyl]acetate, b1·5 218°, which is hydrolyzed with NaOH in water to give a mixture of α-(1-m-chloro)benzyl-3-indazolyl]oxyacetic acid (VI), and α-[1-(m-chloro)benzyl-3-oxo-2-indazolyl]acetic acid (VII). This mixture is treated with EtOH to dissolve VI, leaving the insol VII. The EtOH solution is evaporated to give VI, m. 109° (hexane). Propiolactone (11.7 g.) is added to a solution of 25 g. II and 3 g. NaOH in 75 cc. water heated at 65-70°. The mixture is heated 15 min. more, cooled, and acidified to give 15 g. β-(1-benzyl-3-indazolyl)-oxypropionic acid, m. 135°. HNO3 (d. 1.52) (3.4 cc.) is added to a mixture of 20 g. IV and 200 cc. Ac2O cooled at 0°. The mixture is stirred for 3 hrs. to give α-(1-benzyl-5-nitro-3-indazolyl)oxyacetic acid (VIII), m. 155°. VIII (14 g.) is reduced with a solution of 30 g. SnCl2.H2O in 30 cc. concentrated HCl heated at 80° to give α-(5-amino-1-benzyl-3-indazolyl)oxyacetic acid (IX), m. 127° (decomposition). A solution of 6 g.

IX in 24 cc. Ac2O is heated for 15 min. at 110°, poured into 100 cc. water, alkalized with aqueous Na2CO3, and worked up to give α-(5-acetamido-1-benzyl-3-indazolyl)oxyacetic acid, m. 238°. NaNO2 (6 g.) is added to a solution of 6 g. N-(2,6-dimethyl-3-dimethylsulfamoyl)phenylanthranilic acid in 42 cc. AcOH, the mixture left overnight, and poured into water to give N-(2,6-dimethyl-3-dimethylsulfamoyl)phenyl-N-nitrosoanthranilic acid (X), m. 139° (decomposition). A solution of 10 g. X in 100 cc. AcOH is added to a mixture of 5.7 g. Zn powder and 22 cc. water. The mixture is stirred 2 hrs., heated at 80° for 10 min., and poured into water to give 1-(2,6-dimethyl-3-dimethylsulfamoyl)phenyl-3-hydroxyindazole (XI), m. 182°. A mixture of 1 mole sodium salt of XI, 1.1 moles ClCH2CO2Na, and 11 parts xylene is refluxed for 4-5 hrs. to give α-[1-(2,6-dimethyl-3-dimethylsulfamoyl)phenyl-3-indazolyl]oxyacetic acid, m. 120-1°. Similarly prepared were (m.p. given): α-(1-phenyl-3-indazolyl)oxyacetic acid, 164°; 1-(m-chloro)phenyl-3-hydroxyindazole, 240°; α-[1-(m-chloro)phenyl-3-indazolyl]oxyacetic acid, 148°; 1-(m-trifluoromethyl)phenyl-3-hydroxyindazole, 203°; α-[1-(m-trifluoromethyl)phenyl-3-indazolyl]oxyacetic acid, 156°; α-[1-(o-chloro)benzyl-3-indazolyl]oxyacetic acid, 156°; α-(1-benzyl-6-chloro-3-indazolyl)oxyacetic acid, 157°; α-[1-(2,6-dimethyl)phenyl-3-indazolyl]oxyacetic acid, 130°; α-(1-(2,3-dimethyl)phenyl-3-indazolyl]oxyacetic acid, 142°; β-(1-phenyl-3-indazolyl)oxypropionic acid, 131°; β-(3-indazolyl)-oxypropionic acid, 170°; β-[1-(p-fluoro)phenyl-3-indazolyl]-oxypropionic acid, 150-2°; 1-(p-fluoro)phenyl-3-hydroxyindazole, 250°; 1-(m-bromo)phenyl-3-hydroxyindazole, 242°; β-[1-(m-bromo)phenyl-3-indazolyl]oxypropionic acid, 89°; β-(5-methoxy-3-indazolyl)oxypropionic acid, 184°; (5-chloro-1-benzyl - 3 - indazolyl)oxyacetic acid, 158°; β - (1 - (2,6-dimethyl)-phenyl-3-indazolyl)oxypropionic acid, 133°; and α-(5-amino-1-benzyl-3-indazolyl)oxyacetic acid-HCl, 230°.

IT 23864-74-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23864-74-6 HCAPLUS

CN Anthranilic acid, N-[3-(dimethylsulfamoyl)-2,6-xylyl]-N-nitroso- (8CI) (CA INDEX NAME)